What is claimed is:

1. A method for determining three dimensional structure of a nucleic acid comprising:

(a) providing a chimeric version of said nucleic acid having at least one modified subunit in a preselected position of the chimera;

(b) ionizing said nucleic acid hybrid in a mass spectrometer to provide one or more ions of said chimera;

(c) fragmenting at least one of said ions;

(d) collecting fragmentation data from said fragmentation; and

(e) relating said fragmentation data to said three dimensional structure.

2. The method of claim 1 wherein said relating of fragmentation data comprises identification of the fragmentation pattern of said ions.

3. The method of claim 1 wherein said three-dimensional structure comprises a secondary or tertiary structures.

4. The method of claim 1 wherein said three dimensional structure comprises at least one mismatched base pair, loop, bulge, kink or stem structure.

5. The method of claim 1 wherein said nucleic acid is RNA.

6. The method of claim 5 wherein said nucleic acid corresponds to a 16S rRNA A-site.

7. The method of claim 1 wherein said nucleic acid chimera comprises RNA having one or more deoxynucleotides at said preselected positions.

8. The method of claim 1 wherein said chimera comprises RNA or DNA having a nucleic acid analog moieties at said preselected positions.

9. The method of claim 1 wherein said ionizing of said chimera is achieved through electrospray ionization, atmospheric pressure ionization or matrix-assisted laser desorption

ionization.

10. The method of claim 1 wherein said ion fragmentation takes place within a mass spectrometer capable of performing quadrupole, triple quadrupole, magnetic sector, ion trap, ion cyclotron resonance or time-of-flight mass spectrometry.

11. The method of claim 1 wherein said ion fragmentation involves collision-induced dissociation.

12. The method of claim 1 wherein said ion fragmentation involves infrared multiphoton dissociation.

13. A method for identifying a binding site for a ligand on a biomolecular target comprising:

(a) collecting mass spectral fragmentation data for said biomolecular target;

(b) providing a complex of said biomolecular target and said binding agent;

(c) ionizing said complex in a mass spectrometer to provide one or more ions of said complex;

(d) fragmenting at least one of said ions deriving from the complex;

(e) collecting fragmentation data from said fragmentation of the ions from the complex; and

(f) relating the fragmentation data of the ions of the complex with the fragmentation data from the biomolecular target to determine said site of binding.

14. The method of claim 13 wherein said biomolecular target is a nucleic acid.

15. The method of claim 13 wherein said biomolecular target is RNA.

16. The method of claim 15 wherein said RNA corresponds to a 16S rRNA A-site.

17. The method of claim 14 wherein said nucleic acid includes at least one non-native

nucleotide or nucleotide analog at preselected positions thereof.

18. The method of claim 17 comprising DNA at said preselected positions of an RNA.

19. The method of claim 13 wherein said biomolecular target is a peptide, protein, antibody, carbohydrate, oligosaccharide or glycopeptide.

20. The method of claim 13 wherein said biomolecular target is a nucleic acid moiety.

21. The method of claim 13 wherein said mass spectral fragmentation data for said biomolecular target is provided by:

(i) ionizing said biomolecular target in a mass spectrometer to provide one or more ions of said biomolecular target; and

(ii) fragmenting in a mass spectrometer at least one of said ions.

22. The method of claim 13 wherein said ionizing of said complex is achieved through electrospray ionization, atmospheric pressure ionization or matrix-assisted laser desorption ionization.

23. The method of claim 13 wherein said ion fragmentation takes place within a mass spectrometer capable of performing quadrupole, triple quadrupole, magnetic sector, ion trap, ion cyclotron resonance or time-of-flight mass spectrometry.

24. The method of claim 13 wherein said ion fragmentation involves collision-induced dissociation.

25. The method of claim 13 wherein said ion fragmentation involves infrared multiphoton dissociation.

26. The method of claim 13 wherein said complex is provided by combining together said biomolecular target and said binding agent.

27. A method for determining the relative binding affinity of a binding agent for a biomolecular target comprising:

(a) providing a first complex of said biomolecular target and said binding agent;

(b) ionizing said first complex in a mass spectrometer to provide one or more ions of said first complex;

(c) collecting mass spectral data from the ionization of step (b) and identifying therefrom the ion abundance of said first complex;

(d) providing a second complex of said biomolecular target and a standard binding compound which binds to said target;

(e) ionizing said second complex in a mass spectrometer to provide one or more ions of said second complex;

(f) collecting mass spectral data from the ionization of step (e) and identifying therefrom the ion abundance of said second complex, wherein the relative the ion abundances of said first and second complexes affords a measure of said relative binding affinity.

28. The method of claim 27 wherein said ion abundances of said first and second complexes are compared to identify said relative binding affinity.

29. The method of claim 27 wherein said biomolecular target is a nucleic acid.

30. The method of claim 29 wherein said nucleic acid is RNA.

31. The method of claim 30 wherein said RNA corresponds to a 16S rRNA A-site.

32. The method of claim 30 wherein said RNA includes one or more deoxynucleotide subunits at preselected locations thereof..

33. The method of claim 27 wherein said biomolecular target is a peptide, protein, antibody, carbohydrate, oligosaccharide or glycopeptide.

34. The method of claim 27 wherein said biomolecular target is a nucleic acid moiety.

35. The method of claim 27 wherein said ionizing is achieved through electrospray ionization, atmospheric pressure ionization or matrix-assisted laser desorption ionization.

36. A method for identifying a compound which binds to a preselected biomolecular target, said compound being present in a mixture of compounds comprising:

(a) providing a complex of said biomolecular target and a standard binding compound which binds to said target under conditions effective to achieve said binding;

(b) combining with said complex under competitive binding conditions the mixture of compounds;

(c) ionizing said combination in a mass spectrometer to provide a plurality of ions;

(d) fragmenting at least one of said ions in a mass spectrometer;

(e) collecting mass spectral data for the fragmentation; and

(f) relating said mass spectral data to the existence and degree of competitive binding.

37. The method of claim 36 wherein said biomolecular target is a nucleic acid.

38. The method of claim 37 wherein said nucleic acid is RNA.

39. The method of claim 38 wherein said RNA includes one or more deoxynucleotides at preselected locations thereof.

40. The method of claim 36 wherein said biomolecular target is a peptide, protein, antibody, carbohydrate, oligosaccharide or glycopeptide.

41. A method for identifying a compound which binds to a preselected biomolecular target, said compound being present in a mixture of compounds comprising:

(a) providing a complex of said biomolecular target and a standard compound which binds to said target under conditions effective to achieve said binding;

(b) acquiring fragmentation data from the mass spectrometric analysis of the

complex;

(c) combining with a further portion of said complex under competitive binding conditions the mixture of compounds;

(d) ionizing said combination in a mass spectrometer to provide a plurality of ions;

(e) fragmenting at least one of said ions in a mass spectrometer;

(f) collecting mass spectral data for the fragmentation; and

(g) relating the mass spectral data acquired in steps (b) and (f) to the existence and degree of competitive binding of said compound.

42. A method for identifying in a combinatorial mixture compounds which bind to a biomolecular target, wherein the method comprises:

(a) providing mass spectral data on the ion abundance for said biomolecular target;

(b) providing a first complex of said biomolecular target and a standard binding compound which binds to said target;

(c) combining with said first complex a combinatorial mixture of compounds;

(d) ionizing in a mass spectrometer said combination from step © to provide a plurality of ions for said combination;

(e) collecting from the ionization of step (d) mass spectral data on the ion abundance of said first complex, wherein said ion abundances in steps (a) and (e) affords information for effecting said determination .

43. The method of claim 42 wherein mass differences in the mass spectral data from steps (a) and (e) are identified for determining the mass of compounds from the combinatorial mixture which preferentially bind with said bimolecular target.

44. The method of claim 42 wherein said biomolecular target is a nucleic acid.

45. The method of claim 44 wherein said nucleic acid is RNA.

46. The method of claim 45 wherein said RNA corresponds to a 16S rRNA A-site.

47. The method of claim 45 wherein said RNA includes one or more deoxynucleotide subunits at preselected locations thereof.

48. The method of claim 47 wherein said biomolecular target is a peptide, protein, antibody, carbohydrate, oligosaccharide or glycopeptide.

49. A method for identifying binding sites of a biomolecular target for compounds from a combinatorial library comprising:

(a) providing mass spectral fragmentation data for said biomolecular target;

(b) providing a first complex of said biomolecular target and a standard binding compound which binds to said target;

(c) combining with said first complex a combinatorial mixture of compounds;

(d) ionizing in a mass spectrometer said combination from step © to provide a plurality of ions for said combination;

(e) fragmenting at least one of said ions in a mass spectrometer to generate fragmentation data;

(f) relating the fragmentation data collected for said biomolecular target and the ionized combination from step (d) to afford said identification.

50. The method of claim 49 wherein said mass spectral data for said biomolecular target and said combination are compared to identify said binding sites.

51. The method of claim 49 wherein said biomolecular target is a nucleic acid.

52. The method of claim 51 wherein said nucleic acid is RNA.

53. A method for determining the relative binding affinity of compounds in a combinatorial mixture for a biomolecular target comprising:

(a) providing a first complex of said biomolecular target and a standard binding

compound which binds to said target;

(b) combining with said first complex a combinatorial mixture of compounds, wherein one or more of said compounds from said combinatorial mixture preferentially binds with said biomolecular target to provide secondary complexes;

(c) ionizing said combination of step (b) in a mass spectrometer to provide a plurality of ions;

(d) collecting mass spectral data from the ionization of step © and identifying therein ion abundances for said first and said secondary complexes, wherein the ion abundances of said first and additional complexes affords information for identifying said relative binding affinity.

54. The method of claim 53 wherein said ion abundances of said first and additional complexes are compared to identify said relative binding affinity.

55. The method of claim 53 wherein said biomolecular target is a nucleic acid.

56. A method for screening a plurality of biomolecular targets against a binding agent comprising:

(a) providing n different biomolecular targets, wherein n is an integer greater than or equal to 2;

(b) modifying $n-1$ of said biomolecular targets with mass modifying tags, wherein the mass to charge ratio of ions of about the same charge of said modified biomolecular targets are substantially distinguishable by mass spectrometry;

(c) combining said modified biomolecular targets with a binding agent;

(d) ionizing said combination from step © in a mass spectrometer to provide a plurality of ions; and

(e) collecting mass spectral data from the ionization of step (d) and identifying therefrom ion abundances of said modified biomolecular targets and any complexes formed between said binding agent and said modified biomolecular targets, wherein said ion abundances afford information for effecting said screening.

57. The method of claim 56 wherein the ion abundances of said ions of said modified biomolecular target and said complexes are compared to determine the selectivity of the binding interaction between said ligand and said targets.

58. The method of claim 56 wherein said biomolecular target is a nucleic acid.

59. The method of claim 56 wherein said mass modifying tags are polymeric

60. The method of claim 59 wherein said polymers are a polyethylene glycol, polypropylene, polystyrene, cellulose, sephadex, dextran, peptide or polyacrylamide.

61. The method of claim 59 wherein said mass modifying tag is attached to the 3'-terminus, 5'-terminus or sugar-phosphate backbone of said biomolecular targets.

62. A method for screening a plurality of biomolecular targets against a combinatorial library of compounds comprising:

(a) providing n different biomolecular targets, wherein n is an integer greater than or equal to 2;

(b) modifying $n-1$ of said biomolecular targets with mass modifying tags, wherein the mass to charge ratio of ions of about the same charge of said modified biomolecular targets are substantially distinguishable by mass spectrometry;

(c) combining said modified biomolecular targets with said combinatorial library of compounds;

(d) ionizing said combination from step © in a mass spectrometer to provide a plurality of ions; and

(e) collecting mass spectral data from the ionization of step (d) and identifying therefrom ion abundances of said modified biomolecular targets and any complexes formed between said compounds and said modified biomolecular targets, wherein said ion abundances afford information for effecting said screening.

63. The method of claim 62 wherein the ion abundances of said ions of said modified

biomolecular target and said complexes are compared to determine the selectivity of the binding interactions between said compounds and said targets.

64. The method of claim 62 wherein said biomolecular target is a nucleic acid.

65. The method of claim 62 wherein said mass modifying tags are polymeric.

66. The method of claim 62 wherein said mass modifying tag is attached to the 3'-terminus, 5'-terminus or sugar-phosphate backbone of said biomolecular targets.

67. A method of screening multiple biomolecular targets against a ligand comprising:

(a) providing at least two biomolecular targets which possess different masses such that the mass to charge ratio of ions of about the same charge of said biomolecular targets are substantially distinguishable by mass spectrometry;

(b) combining said bimolecular targets with said ligand;

(c) ionizing said combination of step (b) in a mass spectrometer to form a plurality of ions; and

(d) collecting mass spectral data from the ionization of step © and identifying therefrom ion abundances of said biomolecular targets and any complexes formed between said ligand and said biomolecular targets, wherein said ion abundances afford information for effecting said screening.

68. The method of claim 67 wherein said ion abundances of said biomolecular target and said complexes are compared to determine the selectivity of the binding interactions between said bimolecular targets and said ligand.

69. The method of claim 67 wherein said biomolecular target is a nucleic acid.

70. The method of claim 67 wherein said nucleic acid is derived from prokaryotic or eukaryotic nucleic acids.

71. The method of claim 67 wherein said biomolecular targets comprise a mixture of proteins.

72. A method for determining the nature and extent of binding of a ligand with a molecular interaction site of a biomolecule comprising

contacting the biomolecule with the ligand under conditions selected to promote binding of the ligand to the molecular interaction site to give rise to a complex of said biomolecule and the ligand;

ionizing the complex in a mass spectrometer;

fragmenting the ionized complex; and

determining whether the ligand binds to the molecular interaction site and, if so, determining the strength of binding of such ligand as compared to other ligands bound to said molecular interaction site.

73. The method of claim 72 wherein said biomolecule is RNA.

74. The method of claim 72 wherein said ionization is electrospray ionization.

75. The method of claim 72 wherein said ligand is part of a library of compounds and said binding takes place in the presence of other members of the library.

76. The method of claim 72 wherein said fragmentation comprises collisional activated dissociation or infrared multiphoton dissociation.

77. The method of claim 72 wherein said determining comprises Fourier transform ion cyclotron resonance mass spectroscopy.

78. A method of identifying chemical ligands which bind with high specificity and affinity to a molecular interaction site of an RNA comprising

preparing a library of ligands in accordance with a ranked hierarchy of such ligands predicted or calculated to be bindable to the molecular interaction site;

contacting the RNA with the ligand library under conditions selected to promote binding of the ligand library to the molecular interaction site of the RNA to give rise to complexes of said RNA and the ligands of the library;

ionizing the complexes in a mass spectrometer;

fragmenting the ionized complexes; and

determining whether the ligand of each such complex binds to the molecular interaction site of the RNA and, if so, determining the strength of binding of such ligand as compared to the binding strength of other ligands of the library.

79. The method of claim 78 wherein said ionization is electrospray ionization.

80. The method of claim 78 wherein said fragmentation comprises collisional activated dissociation or infrared multiphoton dissociation.

81. The method of claim 78 wherein said determining comprises Fourier transform ion cyclotron resonance mass spectroscopy.

82. The method of claim 13 wherein said binding site is a metal ion binding site.

83. The method of claim 82 wherein said metal ion is an alkali metal or alkaline earth metal.

84. The method of claim 83 wherein said metal ion is selected from the group consisting of Na^{+}, Mg^{++}, and Mn^{++}.

85. The method of claim 49 wherein said binding site is a metal ion binding site.

86. The method of claim 85 wherein said metal ion is an alkali metal or alkaline earth metal.

87. The method of claim 86 wherein said metal ion is selected from the group consisting

of Na^{+}, Mg^{++}, and Mn^{++}.

88. The method of claim 13 further comprising determining the absolute binding affinity of at least one binding agent and biomolecular target.

89. The method of claim 49 further comprising determining the absolute binding affinity of at least one binding agent and biomolecular target.

90. A method for identifying in a chemical mixture of compounds which bind to a biomolecular target, comprising:

(a) providing mass spectral data on the ion abundances for a blend of the mixture and an excess of said target;

(b) calibrating the mass spectral data by reference to the multiple isotop peaks for the uncomplexed target;

(c) determining the exact mass shift of mass spectral data representing a subset of said compounds complexed with said target to ascertain the exact molecular weight of said complexed compounds.

91. The method of claim 90 further comprising:

(d) identifying the compounds from among those comprising the chemical mixture by reference to their exact molecular weights.

92. The method of claim 91 further comprising establishing a relational database to hold information collected in said determining and identifying steps.

93. The method of claim 92 further comprising determining the binding affinity of the compounds found to bind to said target and including said binding affinity data in said database.

94. The method of claim 93 further comprising selecting from among said compounds found to bind to said target, those having relatively high binding affinity.